

Ce(IV) Oxidation of Cyclopentanone, Cyclohexanone, Cycloheptanone, Cyclooctanone, Acetone, Butanone, Acetoacetic Ester & Benzoylacetone

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Kinetics of oxidation of a series of cycloalkanones such as cyclopentanone, cyclohexanone, cycloheptanone and cyclooctanone and of aliphatic ketones like acetone, butanone, acetoacetic ester and benzoylacetone by Ce(IV) in HClO₄ medium are reported. The order of reactivity among the cyclic ketones is cyclohexanone > cyclooctanone > cycloheptanone ~ cyclopentanone, and among the aliphatic ketones is benzoylacetone > acetoacetic ester > butanone > acetone. The oxidation of cyclohexanone and the aliphatic ketones involves a free-radical mechanism.

KINETICS of oxidation of cyclohexanone by Ce(IV) has been studied earlier by Littler¹ who postulated that the keto-form is directly attacked after it forms a complex with Ce(IV). Shorter and coworkers^{2,3} and Santappa⁴ have shown the formation of Ce(IV)-ketone complex while studying the kinetics of oxidation of certain aliphatic ketones. However, no attempt has been made so far to correlate structure and reactivity of these substrates. Hence, it was thought worthwhile to investigate the oxidation of a series of cyclic ketones such as cyclopentanone, cyclohexanone, cycloheptanone, cyclooctanone as well as of acetone, butanone, acetoacetic ester and benzoylacetone in aq. acetic acid containing 0.05, 0.1 and 0.15M HClO₄ to establish correlation if any, between structure and reactivity of the ketones and to throw light on the mechanism of the reaction.

Materials and Methods

Ceric ammonium nitrate and perchloric acid used were of T. Baker (analysed) grade. Acetic acid (analar BDH) was used as the solvent. The ketones were of either AR or GR grade. For each run about 0.02M Ce(IV) solution containing the required amount of HClO₄ was prepared and standardized by adding a known excess of the standard ferrous ammonium sulphate solution followed by back-titration of the unused Fe(II) against standard dichromate using N-phenylanthranilic acid as the indicator. The substrate solution was prepared in aq. acetic acid. Ce(IV) and the substrate solutions (50 ml each) were equilibrated for 2 hr at the required temperature and mixed. Aliquots (5 ml) of the reaction mixture were taken out at different intervals and treated with 10 ml of standard ferrous ammonium sulphate. The unused Fe(II) was determined as described above.

Results and Discussion

The oxidation reactions are first order each in substrate and the oxidant, and hence the total order

of the reaction is two at a constant [H⁺]. The first and second order rate constants for the cyclic ketones are given in Table 1.

Under the experimental conditions the reaction mixture in the case of cyclohexanone developed a pink colour which is probably due to the formation of a complex of 2-hydroxycyclohexanone, an intermediate compound formed in the oxidation process. Hence, it can be safely presumed that the reactions are clean one-step processes and the kinetics are not

TABLE 1 — RATE CONSTANTS FOR THE OXIDATION OF CYCLIC KETONES

{[Ce(IV)] = 5.0 × 10⁻³M; [HClO₄] = 0.05M; solvent, HOAc-water (40:60, v/v); temp., 35°C}

[Substrate] M	10 ³ k ₁ (min ⁻¹)	10 ³ k ₂ (litre mole ⁻¹ . min ⁻¹)*
CYCLOHEXANONE		
0.075	23.0	30.7
0.1005	33.9	33.9
0.2002	66.1	33.0
0.2512	81.9	32.8
CYCLOPENTANONE		
0.06425	3.78	5.88
0.0753	4.35	5.77
0.1001	5.6	5.63
CYCLOHEPTANONE		
0.06505	3.50	5.40
0.07505	4.20	5.6
0.1001	5.62	5.60
CYCLOOCTANONE		
0.01534	2.40	15.90
0.024895	3.34	13.50
0.03833	5.14	13.40

*k₂ = k₁/[Substrate].

complicated by any subsequent steps which might occur due to oxidation of the 2-hydroxy ketone. However, in the presence of excess Ce(IV), the pink colour of the reaction mixture is not observed. This is understandable as the 2-hydroxy compound immediately after its formation is oxidized further by the oxidant. Hence, in the presence of excess ketone the oxidation product is 2-hydroxy ketone. 2-Hydroxy ketone has also been obtained as the product in the oxidation of cyclohexanone by Mn(III) pyrophosphate⁵.

Effect of varying [substrate] — Plots of $1/k_1$ versus $1/[\text{ketone}]$ are linear and pass through the origin indicating that no complex is formed initially between cyclic ketones and Ce(IV), unlike in the oxidation of acetone by Ce(IV).

Effect of structure on the reactivity of cyclic ketones — An examination of Table 1 reveals that the order of reactivity among the cyclic ketones is cyclohexanone > cyclooctanone > cyclopentanone ~ cycloheptanone. The higher reactivity of cyclohexanone requires explanation. It is quite possible that the terminal hydrogen of the nearly strainless puckered residue $(\text{CH}_2)_4$ in cyclohexene fulfils the stereochemical requirements for hyperconjugation with the cyclic C=C better than does the terminal hydrogen of the nearly flat residue, $(\text{CH}_2)_3$ in cyclopentene.

The order observed shows that even membered cyclic ketones (C_6 and C_8) react much faster than the odd membered ketones (C_5 and C_7). It is interesting to recall the similar differences between the spectra of the even and odd membered ketones. For even membered ketones, the spectrum changes suddenly at the melting point, while in the rest of the temperature range only slight changes are observed. For odd membered ring ketones the spectrum also changes, not at the melting point but at a transition point which lies lower than the melting point. The change in spectrum may be attributed to the possible disappearance of one or more conformations at a given temperature. It is generally presumed that the most favoured conformation of cycloheptanone is the twist chair form⁶ which is responsible for the lowest rate of oxidation. Similarly the lower reactivity of cyclopentanone can be attributed to the existence of cyclopentanone in the half chair form (stable conformation) which has greater symmetry⁷. However, the reactivity of the medium-sized rings are known to alternate as is evidenced from the process involving $\text{Sp}^3 \rightarrow \text{Sp}^2$ conversions, such as solvolysis of cycloalkyl chlorides, acetylation of cycloalkyl tosylates and reactions of cycloalkyl bromides with lithium or potassium iodides⁸. Strictly speaking the observed reactivity of a series of medium-sized cyclic derivatives depends mainly on their conformations.

Reactivity of aliphatic ketones — The second order rate constants (k_2) for Ce(IV) oxidation of aliphatic ketones, namely acetone, butanone, benzoylacetone and acetoacetic ester in aq. acetic acid (40% v/v) are given in Table 2. The order of reactivity is benzoylacetone > acetoacetic ester > butanone > acetone. In the aliphatic ketones studied, it can be presumed that the stability of enols which are

TABLE 2 — SECOND ORDER RATE CONSTANTS (k_2) FOR OXIDATION OF ALIPHATIC KETONES

[Solvent, 1:1 OAc-w.ter (40:60 v/v); temp., 35°]

$[\text{H}_2\text{CeO}_4]$ M	k_2 (litre mole ⁻¹ min ⁻¹) for			
	Acetone	Butanone	Acetoacetic ester	Benzoylacetone
0.025	0.0164	0.0424	3.134	112.86
0.050	0.0182	0.0571	3.674	124.90
0.100	—	—	4.366	152.70
0.150	0.022	0.0725	—	—

TABLE 3 — SECOND ORDER OXIDATION RATES OF CYCLIC KETONES

[Solvent, 1:1 OAc-w.ter (40:60, v/v); temp., 35°]

$[\text{H}_2\text{CeO}_4]$ M	k_2 (litre mole ⁻¹ min ⁻¹) for			
	Cyclohexanone	Cyclopentanone	Cycloheptanone	Cyclooctanone
0.05	0.341	0.0576	0.0553	0.143
0.10	0.441	0.105	0.0988	0.205
0.15	1.303	0.158	0.1700	0.377

likely to be formed in a rapid step depends on two factors: (a) the inductive effect of the electronegative carboxy or benzoyl group which loosens the adjacent proton thereby reducing the relative thermodynamic stability of the keto-form, and (b) the conjugation effect of the unsaturated carboxy or benzoyl group demanding a suitably situated double bond and thus increasing the relative thermodynamic stability of the enol-form. The greater reactivity of the benzoyl group over the carboxy group is mainly due to factor (b). Hence the stability and the percentage of enol-form are the highest in the case of benzoylacetone with the result that it has a maximum reactivity. In simple aliphatic ketones, an increase in the number of alkyl groups increases the rate as alkyl groups are known to increase the equilibrium enol contents. This indicates a dominating hyperconjugative effect of alkyl groups.

ρ - σ^ plot for aliphatic series* — Employing the Taft substituent constants (σ^*) as given below, an attempt has been made to correlate structure and reactivity:

Substituent	σ^* (Taft)
$-\text{CH}_2\text{COO}^-$	0.50
$-\text{CH}_2\text{COC}_6\text{H}_5$	0.60
$-\text{CH}_3$	0.00

Using the second order rate constants (k_2) for acetone, acetoacetic ester and benzoylacetone, a linear plot was obtained between $\log k_2$ and σ^* which gave a ρ value of +1.2. The data for butanone could not be used as there was no Taft substituent constant which could take into account the conjugative ability of the alkyl group.

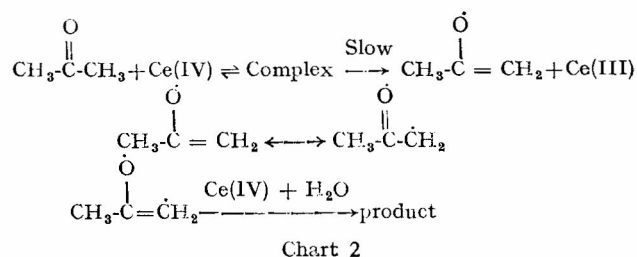
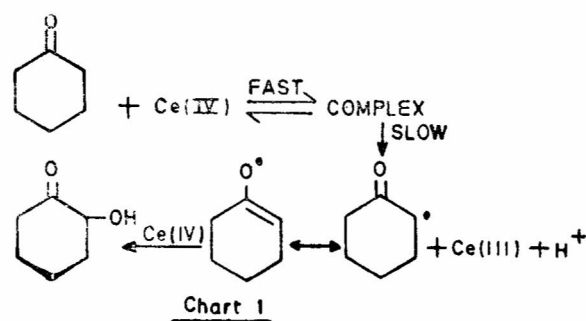
Effect of varying acidity — The rate of oxidation of cyclic ketones increases with increasing $[\text{HClO}_4]$ as seen from Table 3. The plots of $\log k_2$ versus

$[H^+]$ are fairly linear but the plots of $\log k_2$ versus H_0 are better with unit slope. In the case of aliphatic ketones the increase in rate with increasing acidity is marginal in 40% HOAc as seen from Table 2. However, the oxidation of acetone and butanone by Ce(IV) carried in aq. medium at higher ranges of acidity showed that the rate increases with increasing acidity as seen from Table 4. The plots of $\log k_2$ versus H_0 are linear in these cases also, but with a slope of 0.5 only. The different Zucker-Hammett slopes obtained in the case of cyclic and aliphatic ketones suggest that these are dependent on the nature of the substrate. Such a dependence of acidity on the nature of the substrate does not seem to be unusual⁹.

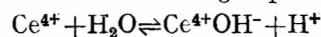
Polymerization of acrylamide — The reaction mixture containing cyclohexanone or aliphatic ketone when allowed to stand with a pinch of acrylamide became turbid and within a few hours the entire mixture turned viscous, thus showing that the oxidation process involves a free radical mechanism. The formation of a free radical is consistent with the low ρ value observed for aliphatic ketones.

Effect of added Ag^+ on the oxidation of butanone — As seen from Table 5 an increasing concentration of $[Ag^+]$ increases the second order rate constant of butanone. The plot of $\log k_2$ versus $[Ag^+]$ is linear but the slope is only fractional. This indicates that the acceleration is only marginal and the rate law is not influenced by the presence of Ag^+ ions. Further it can be concluded that the reactant species are not ion-ion type and no adduct formation takes place¹⁰. The observed marginal increase in rate may be traced to the positive salt effect of added $AgNO_3$.

Nature of the reactive species of Ce(IV) — Hardwick and Robertson¹¹ have demonstrated the existence of Ce(IV) as $Ce(OH)^{3+}$ in addition to free Ce(IV) ions in $HClO_4$. The ranges of $[Ce(IV)]$ and $[H^+]$ used are such that the participation of dimer



in the oxidation process is ruled out. Further, if $Ce(OH)^{3+}$ is considered important, an inverse proportionality between $[H^+]$ and rate would have been observed due to the following equilibrium:



But the rate constant has been found to be directly proportional to $[H^+]$. Hence the reactive species in the oxidation processes studied is free Ce(IV).

Mechanism of oxidation of cyclic ketones — The first order dependence of the oxidation rate on $[ketone]$ and the linear plots of $1/k_1$ versus $1/[substrate]$ passing through origin indicate that the reaction involves complex formation with low stability constant. Study of the solvent effect by Littler¹ based on ideas put forth by Best *et al.*¹² has established that the oxidation of ketones takes place preferably through the attack of keto-form by the oxidant species breaking the α -C-H bond as has been demonstrated by the primary kinetic isotope effect. Induced polymerization of acrylamide has proved the formation of free radicals in these reactions. In the light of the above information a mechanism (Chart 1) for the oxidation of cyclic ketone has been proposed.

The 2-hydroxyketone formed would, however, be degraded to adipic acid in the case of cyclohexanone by C-C fission which is kinetically not detectable.

Mechanism of oxidation of aliphatic ketones — Shorter and Hinshelwood² and Venkatkrishnan and Santappa⁴ have demonstrated the complex formation in the oxidation of acetone and butanone by Ce(IV) in H_2SO_4 and $HClO_4$ respectively, assuming that the extent of complex formation depends on the nature of ketone and the oxidant. Though the structural features of the substrates studied presently point favourably to the reaction of enol-form with the oxidant in the rate determining step, the solvent isotope effect determined for cyclohexanone if applied to aliphatic series seems to favour the rate determining keto-complex decomposition. Hence we propose the following mechanism (Chart 2) fo

TABLE 4 — SECOND ORDER OXIDATION RATES OF ALIPHATIC KETONES IN AQUEOUS MEDIUM AT 35°

$[HClO_4]$ M	k_2 (litre mole ⁻¹ min ⁻¹) for	
	Acetone	Butanone
0.5	0.180	0.501
1.0	0.210	0.672
1.5	0.316	0.927

TABLE 5 — SECOND ORDER OXIDATION RATES OF BUTANONE IN THE PRESENCE OF Ag^+ IN AQ. MEDIUM

$\{[Butanone] = 0.0098M; [Ce(IV)] = 0.01M; [HClO_4] = 0.50M; \text{temp. } 35^\circ\}$

$[Ag^+]$ M	k_2 (litre mole ⁻¹ min ⁻¹)
0.0005025	0.649
0.0010050	0.759
0.0015075	0.308
0.002010	0.981
0.002510	1.015

Ce(IV) oxidation of aliphatic ketones on analogy with the oxidation of cyclohexanone.

This mechanism (Chart 2) explains the polymerization of acrylamide and the observed kinetics and takes into account the earlier observation that Ce(IV) forms a complex with aliphatic ketones, and is also in conformity with the idea that attack of the keto-form is more probable as proposed by Littler¹ in the oxidation of cyclohexanone by v/v .

Thus, it is difficult to prove either mechanism as the arguments and evidences are in favour of both in all the reactions studied so far.

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